Indian Journal of Psychiatry, 2002,44(2)170-172

STEVENS JOHNSON SYNDROME IN A BIPOLAR PATIENT TREATED WITH LAMOTRIGINE

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ABSTRACT

A male patient with bipolar disorder who developed Stevens Johnson Syndrome following treatment with a combination of sodium valproate and lamotrigine is reported. This case report emphasises the importance of being cautious when such a combination is used in patients with associated medical conditions.

Key words: Stevens- Johnson syndrome, lamotrigine, sodium valproate

Lamotrigine, an anticonvlsant of phenyltriazine class was shown to have positive effects on mood during its clinical development for epilepsy (Smith et al., 1998). Reports of the effectiveness of lamotrigine in treating bipolar disorder appeared in 1994 (Weisler et al., 1994). Since that time there have been reports describing moderate to marked broad spectrum efficacy of lamotrigine in the treatment of depressed, hypomanic, manic and mixed phases of bipolar disorder (Calabrese et al., 1999; Erfuth et al., 1998; Kotler et al., 1998; Fogelson et al., 1997; Labbate et al., 1997).

The most commonly observed adverse effects associated with the use of lamotrigine are dizziness, ataxia, somnolence, headache, diplopia, blurred vision, nausea and rash. Rash usually occurs in two to eight weeks of treatment initiation. (Sussman, 2000). Risk factors for rash are age, combining lamotrigine with valproic acid and exceeding the recommended rate of dose escalation for lamotrigine. Rarely angioedema and Stevens- Johnson syndrome have been reported.

Stevens-Johnson syndrome is an acute, inflammatory polmorphic eruption which is a reaction to many different stimuli. It is characterized by a muco-cutaneous involvement in the form of erythematous macules, papules, vesicles, bullae and erosions. The diagnostic lesions are called "target lesions" which show a central discolouration, a zone of pallor with an outer ring of erythema. The mucous membrane of the eyes, oral cavity and genitalia is involved. (Rook, et al.,1998).

The disease may occur as a primary manifestation of systemic infections, malignant or chronic disease of internal organs or as a reaction to ingested drugs like sulphonamides, penicillins, phenytoin, phenylbutazone and carbamazepine (Rees & Rees, 1984). The following case report describes a bipolar patient who developed this condition solely due to lamotrigine.

Case Report: Mr. G.Y., fifty seven years old married male was admitted with a fortnight history of symptoms suggestive of mania. He had a past history of eight manic and four depressive episodes over a period of twenty-nine years. He was detected to have diabetes mellitus and hypertension four and three years back respectively. Diabetes and hypertension were being controlled with glibenclamide 20 mg before

breakfast and enalapril 5 mg daily till nine months back, when the antidiabetic was changed to metformin 250 mg twice daily.

Onset of illness was twenty-nine years back with a manic episode for which he was hospitalised. The episode was treated with haloperidol. He later had two manic and one depressive episodes. Lithium was initiated eight years back during the fifth episode. It had to be discontiued after one year as the patient had two syncopal attacks. Carbamazepine was introduced in a dose of 600 mg a day but the compliance was poor as the patient would consume alcohol. The patient had to be hospitalised subsequently with manic and depressive episodes (with psychotic features) once every year. During each episode he would switch either from mania to depression or vice versa and would respond only to electroconvulsive therapy.

Nine months back he developed papular rash over the extensor surfaces and oral lesions. Hence carbamazepine was withdrawn and patient was switched on to clonazepam 6 mg a day.

His last admission was four months back with a fifteen days history of symptoms suggestive of mania. Sodium valproate was introduced 600mg a day and was later increased to 1200 mg a day but his manic symptoms remained the same even after two weeks of therapy. Nifedipine 15 mg a day was used as a substitue for enalapril. Dosage of nifedipine could not be increased further as the blood pressure was stabilized. There was no response even after one month of therapy. Electroconvulsive therapy was witheld as the patient had received seven ECT's two months prior to the present admission. Lamotrigine 25 mg a day was added and it was increased to 75 mg a day by the third week. Patient was discharged in the fourth week when the manic symptoms had remitted.

Patient reported to the outpatient Department on the fourth day after discharge with history of rash, discharge from the eyes, dysphagia and haematuria of two days duration. On examination he was found to have temperature 101° F and bilateral inguinal lymphadenopathy. There were bilaterally symmetrical lesions in the form of erythematous papules, papulovesicles, bullae, erosions and target lessions all over the body including the palms and soles. There was thick purulent discharge from both eyes, erosions and ulcers were present in the oral mucous membrane and the lips had thick haemorrhagic crusting. A few erosions and erythematous papules were present on the genitalia. Patient was admitted in the Department of Dermatology. Treatment given included intravenous ofloxacin 400 mg, 12 hourly, chlorpheniramine maleate 50 mg 12 hourly, crystalline insulin according to urine sugar chart and symptomatic treatment for oral mucous membrane lesions and conjuntivitis. Systemic steroids were to be started but his condition deteriorated rapidly and he expired on the second day of admission.

The following were the laboratory investigation reports: Hb-10gm%; TLC-6000/ cumm; N-86%; L-13%; M-1%; platlet count 80,000/ cumm; RBSL-280 mg%. Urine analysis showed albumin ++; sugar ++++; RBCs 8-9/HPF; pus cells 45/HPF; blood urea-65mgs%; serum creatinine 1.2mg%; urine for ketones was negative; serum electrolytes and liver function tests were within normal limits; X-ray chest was normal.

DISCUSSION

Lamotrigine is being used in the treatment of refractory epilepsy since the last six years and rare cases of rash related deaths have been reported in worldwide postmarketing experience. Although a few cases of Stevens Johnson syndrome have been reported in the clinical studies of patients treated with lamotrigine, there are no reported deaths till date. The condition was probably caused by lamotrigine. Our patient was receiving sodium valproate along with lamotrigine which is a known risk factor to develop rash. In addition our patient had medical conditions like septicaemia, urinary tract infection diabetes mellitus and he reported late. All this might have contributed to the non recovery.

The occurrence of such a death cautions us that a combination of lamotrigine and

valproate should be used judiciously in patients with mood disorders having associated medical conditions. The benefits of such a combination are to be weighed against disastrous side effects before starting the therapy.

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